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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,864	BLAKESLEY ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 20-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENT, REMARKS AND STATUS OF THE CLAIMS

1. The amendment and remarks filed 7/2/04 are acknowledged, entered and considered. In view of Applicant's request claims 1-4, 7-18, 20-25, 28, 30, 32-37 have been amended, claims 38-40 have been added and claim 19 has been canceled. Claims 1-18 and 20-40 are now pending in the application. Also, in view of Applicant's request reference AS which is a PCT search report and reference AT2 which is a copending application No. 09/478,456 have been considered. The objections to the abstract and trademarks and the rejections under 35 U.S.C. 112, second paragraph, 35 U.S.C. 102(b) and 35 U.S.C. 103(a) over the prior art of record are withdrawn in view of Applicant's amendment and remarks filed 7/2/04.

The followings are new ground of rejections necessitated by Applicant's amendments:

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18 and 20-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/61603 taken with Yoshioka et al (U.S. Patent No. 4,347,316), Henco et al (U.S. Patent No. 5,652,141) and Shah et al (U.S. Patent No. 4,303,530).

The prior art of WO 99/61603 discloses like the instantly claimed invention methods of separating and isolating proteins or peptide molecules and composition thereof from circular nucleic acid molecules (e.g., bacterial cells) via lysis and/or disruption under alkaline conditions at pH > 8 with a solid matrix consisting essentially of a silica matrix in presence of at least one chaotropic substance and one or more additional isolation procedures, such as filtration and/or chromatographic procedures (See e.g., pages 2, 5, 6, 8 and the examples and protocols) as directed to claims 1-3, 7, 8, 11-17 and 20. On page 9, paragraph 2, the reference states alternatively, plasmid DNA can be purified from the "crude lysate" which can be established by a proteinase K cell-digest, or by an ultra-sonic lysis. The method of the invention is not limited to lysis of cells performed according to alkaline lysis. Thus, clearly suggests the use of

enzymes for lysis/disruption/permeabilization composition, and as such meets the limitations of claims 9 and 10.

Further, Applicant defines "Cell lysing/disrupting/permeablizing compound or composition" as a composition or a component of a composition that effects lysis, rupture, or portion of the cells, tissues, or organisms used as the source of the protein and peptide molecules to be isolated, such that the soluble protein and peptide molecules (or portion thereof) that are contained in the cell, tissue, or organism source are released from the cell, tissue, or organism. According to the invention, the cells, tissues or organisms need not be completely lysed/disrupted/permeabilized, and all of the protein and peptide molecules contained in the source cells, tissues or organisms need not be released therefrom. Preferably, a cell disrupting or cell lysis compound or composition will release at least 25%, 50%, 75%, 80%, 85%, 90%, 95%, 97%, 99%, or more of the total protein or peptide molecules of interest (soluble and insoluble) that are contained in the cell, tissue, or organism (See e.g., page 23, last paragraph to page 24, 1 to 2 of the instant specification). Therefore, in view of the above statement, the reference of WO 99/61603 clearly discloses contacting cells with lysis/disruption/permeabilization composition or compound to effect lysis of the cells.

The primary reference of WO 99/61603 differs from claims 1-18 and 20-40 in not teaching the use of a pore-containing matrix with the pore sizes claimed and an apparatus containing a housing, pore-containing matrix and chromatographic resin and a kit formulation thereof. However, the patent of Yoshioka et al discloses a process for isomerizing a glucose containing solution to covert a part of glucose to fructose by a

method of isomerization in which the separation of fructose from the isomerized glucose solution may be carried out by conventional procedure. That is, the isomerized glucose solution is brought into contact with a matrix such zeolite having pores at least 5 angstroms in average diameter, whereby fructose and glucose contained in the isomerized glucose solution is adsorbed in the zeolite; and then, the adsorbed fructose is eluted from the zeolite particles. Thus, clearly showing the use of a matrix such as zeolite having pores at least 5 angstroms in average diameter (See e.g. col. 8). Further, Shah et al teach the use of a filter for removing microaggregates from the blood and blood components having a pore size and/or diameter of about 400 to microns (See e.g., cols 1-3) as directed to claims 4-6 and 28. Furthermore, the reference of Henco et al on col. 2 and Figure 1 discloses the use of a device having matrix size from 1 to 50 μm in which the cell immobilized with matrix are lysed using detergent and eluted by adjusting to high ionic strength subsequent to various washing operations. Thus, the reference clearly teaches the use of an apparatus containing a housing, a pore-containing matrix and a chromatographic resin as directed to claims 21-32.

Therefore, given the teachings of the primary reference of WO 99/61603, one of ordinary skill in the art would have been motivated to adapt the above scheme of using of a pore-containing matrix and an apparatus containing a housing, pore-containing matrix and a chromatographic resin. Further, such features are known or suggested in the art, as seen in the secondary references, and including such features into methods and compositions for methods of separating and isolating proteins or peptide molecules and composition thereof from circular nucleic acid molecules (e.g., bacterial cells) via

lysis and/or disruption under alkaline conditions of the primary references would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

With respect to the kit, the secondary reference of Henco et al discloses an apparatus containing a housing, a pore-containing matrix and a chromatographic resin; however, from the cited references, it is conventional and within the ordinary skill in the art based upon the teachings of the combined references to have such kits/compositions as set forth in claims 33-37 since the combined references teach using these compositions together in the same formulation that would have been found in the claimed composition and/or kits to formulate compositions into a kit format because the claimed kit is tailored for use in claimed apparatus kit formulation comprising the composition claimed. Hence, it would have been obvious to package the composition required for the method into kit format of the well-known commercial expediency of doing so.

Therefore, the combined teachings of the prior art makes obvious the claimed invention because at the time the invention was made based on the combined teachings of the prior art and for the reasons given above; one of ordinary skill in the art would have easily adapt the already known methods and apparatus and kit formulation thereof for use in methods of separating and isolating proteins or peptide molecules and composition thereof from circular nucleic acid molecules (e.g., bacterial cells) via lysis and/or disruption under alkaline conditions at pH > 8 with a solid matrix consisting essentially of a silica matrix in presence of at least one chaotropic substance and one or

more additional isolation procedures, such as filtration and/or chromatographic procedures; absent of sufficient objective factual evidence or unexpected results to the contrary.

CLAIMS REJECTION-35 U.S.C. 112 [1st] PARAGRAPH.

3. Claims 1-18 and 20-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for separating and/or isolating of protein and peptide from bacterial cells such as *E. coli* by various purification procedures and composition, apparatus and kit formulations thereof, does not reasonably provide enablement for a method for separating and/or isolating of protein and peptide from high molecular weight molecules and structures, wherein said high molecular weight molecules or structures are selected from group consisting of chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates of molecules and inclusion bodies, wherein one or more cells are selected from the group consisting of a bacterial cells, yeast cells, fungal cells, animal cells, insect cells, mammalian cells, human cells, cells infected by a virus, transfected cells and plant cells, wherein one or more cells are bacterial cells of a genus selected from the group consisting of *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudomonas, Serratia and Caryophanon,* and compositions, apparatus and kits formulations thereof as recited in claims 1-18 and 20-40. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification in Examples 1-6 show methods for separating and/or isolating of protein and peptide from bacterial cells such as *E. coli* by various purification procedures and composition, apparatus and kit formulations thereof. Thus, the instant specification demonstrates generally to compositions, methods and kits that are useful in the isolation of protein and peptide molecules from cells via lysis and one or more additional isolation procedures, such as one or more chromatography/filtration separation. However, the scope of the instantly claimed invention are very specific and speculative in that there is/are no working example(s) or data or evidence which shows that the claimed methods for separating and/or isolating of protein and peptide from high molecular weight molecules and structures, wherein said high molecular weight molecules or structures are selected from group consisting of chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates of molecules and inclusion bodies, wherein one or more cells are selected from the group consisting of a bacterial cells, yeast cells, fungal cells, animal cells, insect cells, mammalian cells, human cells, cells infected by a virus, transfected cells and plant cells, wherein one or more cells are bacterial cells of a genus selected from the group consisting of *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudómonas, Serratia and Caryophanon,* and compositions, apparatus and kits formulations thereof in the manner claimed.

There is no evidence in the instant specification fro compositions, methods and kits of the invention are suitable for isolating a variety of proteins and peptide molecules from all kinds of cells in the manner claimed, except for protocols and recitation of various references and incorporating improperly the references to show methods for separating and/or isolating of protein and peptide from high molecular weight molecules and structures, wherein said high molecular weight molecules or structures are selected from group consisting of chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates of molecules and inclusion bodies, wherein one or more cells are selected from the group consisting of a bacterial cells, yeast cells, fungal cells, animal cells, insect cells, mammalian cells, human cells, cells infected by a virus, transfected cells and plant cells, wherein one or more cells are bacterial cells of a genus selected from the group consisting of *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudomonas, Serratia and Caryophanon,* and compositions, apparatus and kits formulations thereof as disclosed on pages 3-40 in the instant specification.

Further, Applicant acknowledges on page 1, last paragraph, by stating that lysis by physical methods produces membrane fragments and small DNA molecules caused by shearing of the chromosomal DNA, either of which can interfere with subsequent analysis of the desired proteins. Removal of these contaminants requires additional costly and time-consuming purification steps. Thus, such statements discourage the employment of compositions, methods and kits that are useful in the isolation of all kinds of protein or peptide molecules from high molecular weight molecules and

structures by contacting all kinds of cells from various sources such as from any bacteria, fungus, yeast, animal, insect, mammalian, human, virus, plant, etc. Therefore, in view of this acknowledgment, there are no sufficient data or evidence to substantiate such protocols of using methods for separating and/or isolating of protein and peptide from high molecular weight molecules and structures, wherein said high molecular weight molecules or structures are selected from group consisting of chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates of molecules and inclusion bodies, wherein one or more cells are selected from the group consisting of a bacterial cells, yeast cells, fungal cells, animal cells, insect cells, mammalian cells, human cells, cells infected by a virus, transfected cells and plant cells, wherein one or more cells are bacterial cells of a genus selected from the group consisting of *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudomonas, Serratia and Caryophanon,* and compositions, apparatus and kits formulations thereof in the manner claimed. Hence, the only support for the claimed methods and kits of the invention are suitable for isolating a variety of proteins and peptide molecules from all kinds of cells in the manner claimed is Applicant's supposition of the invention as recited in the protocols.

Therefore, in view of the above, it would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as specifically claimed is enabled, since a vast range of protein molecule or population of protein or peptide molecules from high

molecular weight molecules and structures in all kinds of possible cells are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which are not present in the specification. Hence, one of ordinary skill in the art would not be able to identify all the methods for separating and/or isolating of protein and peptide from high molecular weight molecules and structures, wherein said high molecular weight molecules or structures are selected from group consisting of chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates of molecules and inclusion bodies, wherein one or more cells are selected from the group consisting of a bacterial cells, yeast cells, fungal cells, animal cells, insect cells, mammalian cells, human cells, cells infected by a virus, transfected cells and plant cells, wherein one or more cells are bacterial cells of a genus selected from the group consisting of *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudomonas, Serratia and Caryophanon,* and compositions, apparatus and kits formulations thereof in the manner claimed to be effective for the claimed purpose as encompassed in the claims would be effective and under what conditions.

Further, the first paragraph of 35 U.S.C. 112 requires, *inter alia*, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable

correlation to the scope of the enablement provided by the specification". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Thus, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data and the breadth of the claims; the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

ACTION IS FINAL, NECESSITATED BY AMENDMENT

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONCLUSION AND FUTURE CORRESPONDENCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272 0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
September 17, 2004